

Protocol Registration Receipt

06/12/2013

Study of Pazopanib and Pemetrexed in Advanced Non-small Cell Lung Cancer

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00871403

► Purpose

The main purpose of this study is to determine whether the combination of pazopanib and pemetrexed is safe and effective in the treatment of advanced non-small cell lung cancer (NSCLC).

Condition	Intervention	Phase
Lung Cancer, Non-Small Cell	Drug: pazopanib and pemetrexed Drug: pemetrexed and cisplatin	Phase 2

Study Type: Interventional

Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study

Official Title: An Open-label, Multicentre, Randomised Phase II Study of Pazopanib in Combination With Pemetrexed in First-line Treatment of Subjects With Predominantly Non-squamous Cell Stage IIIBwet/IV Non-small Cell Lung Cancer

#### Further study details as provided by GlaxoSmithKline:

##### Primary Outcome Measure:

- Progression-free Survival (PFS) [Time Frame: Randomization until progression or death (up to 85 weeks)] [Designated as safety issue: No]  
PFS is defined as the interval between the date of randomization (date on which the investigator evaluated the participant and first determined he/she had disease progression) and the first occurrence of progressive disease (PD) or death from any cause. Per Response Evaluation Criteria in Solid Tumors (RECIST), version 1, PD is defined as a  $\geq 20\%$  increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum longest diameter recorded since the treatment started or the appearance of  $\geq 1$  new lesion).

##### Secondary Outcome Measures:

- Overall Survival (OS) [Time Frame: Randomization until death (up to 85 weeks)] [Designated as safety issue: No]  
OS was determined from the date of randomization to the date of death from any cause. Participants who had not died at the time of the cut-off for the final analysis were censored at the date the participants were last known to be alive. Because enrollment in the study was halted prematurely, the ability to achieve an estimate of OS was compromised. Consequently, OS was not estimated.
- Best Overall Response, Assessed as the Number of Participants With the Indicated Tumor Response: Investigator Assessed Only [Time Frame: Randomization until response or progressive disease (up to 85 weeks)] [Designated as safety issue: No]  
Tumor response was assessed by the Investigator according to the RECIST, version 1.0. A participant was defined as a responder if he/she sustained a complete response (CR; the disappearance of all target lesions) or partial response (PR;  $\geq 30\%$  decrease in the sum of the longest diameter of target lesions) for at least 4 weeks at any time during randomized treatment. Stable disease is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum longest diameter since the treatment started.
- Percentage of Participants With a Complete Response or a Partial Response [Time Frame: Randomization until response or progressive disease (up to 85 weeks)] [Designated as safety issue: No]  
The percentage of participants with a complete response or a partial response was evaluated.

Enrollment: 107

Study Start Date: July 2009

Study Completion Date: March 2011

Primary Completion Date: March 2011

Arms	Assigned Interventions
Experimental: Arm 1 Investigational treatment (pazopanib and pemetrexed)	Drug: pazopanib and pemetrexed oral pazopanib 600 mg once daily and pemetrexed intravenous (IV) 500mg/m <sup>2</sup> once every 3 weeks, then pazopanib 800 mg once daily
Active Comparator: Arm 2 Standard treatment (pemetrexed and cisplatin)	Drug: pemetrexed and cisplatin pemetrexed IV 500 mg/m <sup>2</sup> and cisplatin IV 75 mg/m <sup>2</sup> once every 3 weeks

## ► Eligibility

Ages Eligible for Study: 18 Years and older

Genders Eligible for Study: Both

Inclusion Criteria:

- Written informed consent
- At least 18 years old
- Histologically- or cytologically-confirmed diagnosis of predominantly nonsquamous cell Stage IIIBwet (with confirmed malignant pleural effusion) or Stage IV NSCLC
- No prior systemic first-line therapy for advanced NSCLC
- Measurable disease
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Life expectancy of at least 12 weeks
- Able to swallow and retain oral medication
- Adequate organ system function (hematological, hepatic, and renal)
- Non-childbearing potential (i.e., physiologically incapable of becoming pregnant) OR childbearing potential, and agrees to use adequate contraception. A male with a female partner of childbearing potential is eligible if he uses a barrier method of contraception or abstinence during the study

Exclusion Criteria:

- Active malignancy or any malignancy in the 3 years prior to first dose of study drug other than NSCLC
- Central nervous system (CNS) metastases or leptomeningeal carcinomatosis, except for asymptomatic, previously treated CNS metastases

- Clinically significant gastrointestinal abnormalities
- Prolongation of corrected QT interval (QTc) > 480 msec
- History of any one or more cardiovascular conditions within the past 6 months prior to randomization
- Poorly controlled hypertension
- History of cerebrovascular accident (including transient ischemic attacks), pulmonary embolism or untreated deep venous thrombosis (DVT) within the past 6 months
- Major surgery or trauma within 28 days or any non-healing wound, fracture, or ulcer
- Evidence of active bleeding or bleeding diathesis
- Recent hemoptysis
- Endobronchial lesions and/or lesions infiltrating major pulmonary vessels
- Serious and/or unstable pre-existing medical (e.g., uncontrolled infection), psychiatric, or other condition that could interfere with subject's safety, provision of informed consent, or compliance to study procedures
- Use of any prohibited medication
- Use of an investigational agent within 28 days or 5 half-lives, whichever is longer, prior to the first dose of study drug
- Ongoing toxicity from prior anti-cancer therapy that is >Grade 1 and/or that is progressing in severity except alopecia
- Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to pazopanib, pemetrexed, and/or cisplatin
- Inability to interrupt aspirin or other non-steroidal anti-inflammatory drugs during the study
- Inability or unwillingness to take folic acid, vitamin B12 supplementation, or dexamethasone
- Clinically significant third-space fluid collections (e.g., ascites or pleural effusions) that cannot be controlled by drainage or other procedures prior to study start
- Recent or concurrent yellow fever vaccination

## Contacts and Locations

### Locations

#### Denmark

GSK Investigational Site  
Herlev, Denmark, 2730

#### United Kingdom

GSK Investigational Site  
Sutton, Surrey, United Kingdom, SM2 5PT

### Investigators

## ▶ More Information

Responsible Party: GlaxoSmithKline  
 Study ID Numbers: 111128  
 Health Authority: Spain: Agencia Española del Medicamento y Productos Sanitarios  
 United Kingdom: Medicines and Healthcare Products Regulatory Agency  
 Italy: Azienda Sanitaria Ospedaliera San Luigi Gonzaga  
 Belgium: Agence Fédérale des Médicaments et des Produits de la Santé  
 Germany: Bundesinstitut für Arzneimittel und Medizinprodukte  
 Denmark: Danish Medicines Agency  
 France: Agence Française de Sécurité Sanitaire des Produits de Santé  
 Netherlands: De Centrale Commissie Mensgebonden Onderzoek

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## Study Results

## ▶ Participant Flow

### Pre-Assignment Details

Per protocol, the study had 2 treatment arms: Arm 1, investigational (pazopanib+pemetrexed); and Arm 2, standard of care (cisplatin+pemetrexed). Protocol amendment 1 lowered the pazopanib starting dose (SD) for new Arm 1 participants from 800 to 600 milligrams. For clarity, safety/demography data for these different SDs are presented separately.

### Reporting Groups

	Description
Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 600 milligrams (mg) once daily plus intravenous pemetrexed 500 mg/meters squared (m <sup>2</sup> ) once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase.

	Description
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Combination Treatment Phase

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Started	9	62	35
Completed	0 <sup>[1]</sup>	13 <sup>[2]</sup>	23 <sup>[3]</sup>
Not Completed	9	49	12
Randomized but Not Treated	1	1	1
Treatment Stopped; Protocol Amendment	8	19	0
Adverse Event	0	17	2
Disease Progression	0	8	5

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Withdrawal by Subject	0	3	1
Physician Decision	0	1	3

[1] No participants completed Combination Treatment.

[2] These participants completed combination treatment

[3] These participants completed combination treatment

### Monotherapy Treatment Phase

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Started	0	13	1
Completed	0	0	0
Not Completed	0	13	1
Disease Progression	0	9	1
Adverse Event	0	4	0

## Baseline Characteristics

### Reporting Groups

	Description
Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 600 milligrams (mg) once daily plus intravenous pemetrexed 500 mg/meters squared (m <sup>2</sup> ) once every 3 weeks for 4 or

	Description
	6 cycles during the Combination Treatment Phase.
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Baseline Measures

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	Total
Number of Participants	9	62	35	106
Age, Continuous [units: Years] Mean (Standard Deviation)	60.4 (14.32)	60.8 (8.27)	61.8 (9.35)	61.1 (9.16)
Gender, Male/Female [units: Participants]				
Female	2	23	12	37
Male	7	39	23	69

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	Total
Race/Ethnicity, Customized [units: participants]				
African American/African Heritage	0	1	0	1
Asian - Central/South Asian Heritage	1	0	0	1
White - Arabic/North African Heritage	0	2	2	4
White - White/Caucasian/European Heritage	8	59	33	100

## Outcome Measures

### 1. Primary Outcome Measure:

Measure Title	Progression-free Survival (PFS)
Measure Description	PFS is defined as the interval between the date of randomization (date on which the investigator evaluated the participant and first determined he/she had disease progression) and the first occurrence of progressive disease (PD) or death from any cause. Per Response Evaluation Criteria in Solid Tumors (RECIST), version 1, PD is defined as a $\geq 20\%$ increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum longest diameter recorded since the treatment started or the appearance of $\geq 1$ new lesion).

Time Frame	Randomization until progression or death (up to 85 weeks)
Safety Issue?	No

### Analysis Population Description

Intent-to-Treat (ITT) Population: all participants randomized to receive treatment and who were analyzed based on the assigned randomized treatment and not based on actual treatment received/not received. Participants who had neither progressed nor died were censored at the date of the last adequate tumor assessment at the time of the cut-off.

### Reporting Groups

	Description
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Measured Values

	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Number of Participants Analyzed	62	35
Progression-free Survival (PFS) [units: weeks]	25.0 (17.3 to	22.9 (18.4 to

	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Median (95% Confidence Interval)	34.1)	27.7)

### Statistical Analysis 1 for Progression-free Survival (PFS)

Groups	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup> , Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Method	Log Rank
P-Value	0.2647
Hazard Ratio (HR)	0.75
95% Confidence Interval	0.43 to 1.28

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

The hazard ratios is estimated using a Pike estimator. The estimated value is the hazard ratio comparing Pazopanib 800 mg plus pemetrexed 500 mg/m<sup>2</sup> to Cisplatin 75 mg/m<sup>2</sup> plus pemetrexed 500 mg/m<sup>2</sup>.

## 2. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	OS was determined from the date of randomization to the date of death

	from any cause. Participants who had not died at the time of the cut-off for the final analysis were censored at the date the participants were last known to be alive. Because enrollment in the study was halted prematurely, the ability to achieve an estimate of OS was compromised. Consequently, OS was not estimated.
Time Frame	Randomization until death (up to 85 weeks)
Safety Issue?	No

## Analysis Population Description

ITT Population

### Reporting Groups

	Description
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Measured Values

	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

### 3. Secondary Outcome Measure:

Measure Title	Best Overall Response, Assessed as the Number of Participants With the Indicated Tumor Response: Investigator Assessed Only
Measure Description	Tumor response was assessed by the Investigator according to the RECIST, version 1.0. A participant was defined as a responder if he/she sustained a complete response (CR; the disappearance of all target lesions) or partial response (PR; $\geq 30\%$ decrease in the sum of the longest diameter of target lesions) for at least 4 weeks at any time during randomized treatment. Stable disease is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum longest diameter since the treatment started.
Time Frame	Randomization until response or progressive disease (up to 85 weeks)
Safety Issue?	No

### Analysis Population Description

ITT Population. A participant without a post-baseline assessment of response was considered to be a non-responder; i.e., all randomized participants are included in the denominator.

### Reporting Groups

	Description
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Measured Values

	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Number of Participants Analyzed	62	35
Best Overall Response, Assessed as the Number of Participants With the Indicated Tumor Response: Investigator Assessed Only [units: participants]		
Complete response	0	0
Partial response	14	12
Stable disease	13	14
Progressive disease	6	5

	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Unknown	29	4

#### 4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Complete Response or a Partial Response
Measure Description	The percentage of participants with a complete response or a partial response was evaluated.
Time Frame	Randomization until response or progressive disease (up to 85 weeks)
Safety Issue?	No

#### Analysis Population Description

ITT Population

#### Reporting Groups

	Description
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression

	Description
	participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Measured Values

	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Number of Participants Analyzed	62	35
Percentage of Participants With a Complete Response or a Partial Response [units: percentage of participants]	14	12

### Statistical Analysis 1 for Percentage of Participants With a Complete Response or a Partial Response

Groups	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup> , Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Method	Other [Binomial asymptotic]
P-Value	0.2113
Other Estimated Parameter [percent difference in response]	-12.0
95% Confidence Interval	-30.6 to 7.2

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for

statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

The estimated value is the percent difference in the response rate comparing Pazopanib 800 mg plus pemetrexed 500 mg/m<sup>2</sup> to Cisplatin 75 mg/m<sup>2</sup> plus pemetrexed 500 mg/m<sup>2</sup>.

## ▶ Reported Adverse Events

### Reporting Groups

	Description
Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 600 milligrams (mg) once daily plus intravenous pemetrexed 500 mg/meters squared (m <sup>2</sup> ) once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase.
Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Oral pazopanib 800 mg once daily plus intravenous (IV) pemetrexed 500 mg/ m <sup>2</sup> once every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. If participants experienced no disease progression, unacceptable toxicities, or death during the Combination Treatment Phase, they continued on pazopanib 800 mg monotherapy until disease progression, unacceptable toxicities, or death.
Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>	IV cisplatin 75 mg/m <sup>2</sup> plus intravenous pemetrexed 500 mg/m <sup>2</sup> once daily every 3 weeks for 4 or 6 cycles during the Combination Treatment Phase. Until Protocol Amendment 2, upon disease progression participants had the opportunity to receive pazopanib 800 mg monotherapy if the investigator considered it an appropriate treatment option after considering alternative options for second-line treatment.

### Additional Description

Serious adverse events (SAEs) and non-serious AEs are presented for the entire treatment period (Combination Treatment Phase followed by the Monotherapy Phase). SAEs and AEs were collected in the Safety Population, comprised all participants who had received at least one dose of both drugs within the assigned regimen.

### Serious Adverse Events

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Total # participants affected/at risk	3/8 (37.5%)	34/61 (55.74%)	12/34 (35.29%)
Blood and lymphatic system disorders			
Anaemia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	1/34 (2.94%)
# events			
Febrile bone marrow aplasia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Febrile neutropenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	1/34 (2.94%)
# events			
Leukopenia † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Neutropenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	5/61 (8.2%)	1/34 (2.94%)
# events			
Pancytopenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Thrombocytopenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	0/34 (0%)
# events			
Cardiac disorders			
Acute coronary syndrome † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Cardiac failure † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Cardiovascular disorder † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Gastrointestinal disorders			
Abdominal pain † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	0/34 (0%)
# events			
Abdominal pain upper † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	0/34 (0%)
# events			
Ascites † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Constipation † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	1/34 (2.94%)
# events			
Diarrhoea † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	0/34 (0%)
# events			
Gastrointestinal haemorrhage † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Ileus † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Nausea † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	1/34 (2.94%)
# events			
Pancreatitis † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Rectal haemorrhage † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Vomiting † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	1/34 (2.94%)
# events			
General disorders			
Chills † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Death † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	0/61 (0%)	0/34 (0%)
# events			
Disease progression † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	0/34 (0%)
# events			
Fatigue † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
General physical health deterioration † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Pyrexia † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	1/61 (1.64%)	0/34 (0%)
# events			
Hepatobiliary disorders			
Cholecystitis acute † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Infections and infestations			
Empyema † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Gastroenteritis norovirus † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Lung infection † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Necrotising fasciitis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Pneumonia † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	3/61 (4.92%)	2/34 (5.88%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# events			
Respiratory tract infection † A			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	2/34 (5.88%)
# events			
Sepsis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Injury, poisoning and procedural complications			
Femur fracture † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Pneumonitis chemical † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Investigations			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Alanine aminotransferase increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	5/61 (8.2%)	0/34 (0%)
# events			
Aspartate aminotransferase increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Bilirubin conjugated increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Blood bilirubin increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	0/34 (0%)
# events			
Blood creatinine increased † A			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# events			
Bronchopneumonia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	0/34 (0%)
# events			
Hepatic enzyme increased † A			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	1/34 (2.94%)
# events			
Metabolism and nutrition disorders			
Decreased appetite † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Musculoskeletal and connective tissue disorders			
Back pain † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to peritoneum † A			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Tumour embolism † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Nervous system disorders			
Dizziness † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Spinal cord compression † <sup>A</sup>			
# participants affected/at	0/8 (0%)	0/61 (0%)	1/34 (2.94%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
risk			
# events			
Syncope † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Renal and urinary disorders			
Proteinuria † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Renal failure † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	0/61 (0%)	0/34 (0%)
# events			
Renal failure acute † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	0/34 (0%)
# events			
Reproductive system			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
and breast disorders			
Prostatitis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Respiratory, thoracic and mediastinal disorders			
Dyspnoea † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	1/34 (2.94%)
# events			
Epistaxis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Haemoptysis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Oropharyngeal pain † <sup>A</sup>			
# participants affected/at	0/8 (0%)	1/61 (1.64%)	0/34 (0%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
risk			
# events			
Pleural effusion † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	2/34 (5.88%)
# events			
Pneumothorax † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Pulmonary embolism † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	1/34 (2.94%)
# events			
Vascular disorders			
Deep vein thrombosis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Embolism venous † <sup>A</sup>			
# participants affected/at	0/8 (0%)	0/61 (0%)	1/34 (2.94%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
risk			
# events			
Hypertension † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			
Vasculitis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	0/34 (0%)
# events			

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

## Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Total # participants affected/at risk	7/8 (87.5%)	59/61 (96.72%)	32/34 (94.12%)
Blood and lymphatic system disorders			
Anaemia † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	2/8 (25%)	5/61 (8.2%)	10/34 (29.41%)
# events			
Leukopenia † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	13/61 (21.31%)	3/34 (8.82%)
# events			
Lymphopenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	8/61 (13.11%)	8/34 (23.53%)
# events			
Neutropenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	36/61 (59.02%)	9/34 (26.47%)
# events			
Thrombocytopenia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	6/61 (9.84%)	7/34 (20.59%)
# events			
Thrombocytosis † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	0/61 (0%)	0/34 (0%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# events			
Ear and labyrinth disorders			
Tinnitus † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	4/34 (11.76%)
# events			
Eye disorders			
Conjunctivitis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	2/34 (5.88%)
# events			
Dry eye † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	0/61 (0%)	3/34 (8.82%)
# events			
Lacrimation increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	6/61 (9.84%)	4/34 (11.76%)
# events			
Gastrointestinal			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
disorders			
Abdominal pain † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	10/61 (16.39%)	3/34 (8.82%)
# events			
Abdominal pain upper † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	7/61 (11.48%)	4/34 (11.76%)
# events			
Constipation † <sup>A</sup>			
# participants affected/at risk	2/8 (25%)	7/61 (11.48%)	11/34 (32.35%)
# events			
Diarrhoea † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	21/61 (34.43%)	6/34 (17.65%)
# events			
Dyspepsia † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	5/61 (8.2%)	1/34 (2.94%)
# events			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Flatulence † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	2/34 (5.88%)
# events			
Haemorrhoids † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	1/34 (2.94%)
# events			
Nausea † <sup>A</sup>			
# participants affected/at risk	4/8 (50%)	24/61 (39.34%)	21/34 (61.76%)
# events			
Stomatitis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	4/34 (11.76%)
# events			
Vomiting † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	15/61 (24.59%)	12/34 (35.29%)
# events			
General disorders			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Asthenia † <sup>A</sup>			
# participants affected/at risk	3/8 (37.5%)	7/61 (11.48%)	10/34 (29.41%)
# events			
Fatigue † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	24/61 (39.34%)	10/34 (29.41%)
# events			
Mucosal inflammation † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	10/61 (16.39%)	3/34 (8.82%)
# events			
Non-cardiac chest pain † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	6/34 (17.65%)
# events			
Oedema peripheral † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	0/34 (0%)
# events			
Pain † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	0/61 (0%)	2/34 (5.88%)
# events			
Pyrexia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	7/61 (11.48%)	7/34 (20.59%)
# events			
Infections and infestations			
Nasopharyngitis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	1/34 (2.94%)
# events			
Investigations			
Alanine aminotransferase increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	11/61 (18.03%)	1/34 (2.94%)
# events			
Aspartate aminotransferase increased † <sup>A</sup>			
# participants affected/at	0/8 (0%)	8/61 (13.11%)	1/34 (2.94%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
risk			
# events			
Blood bilirubin increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	0/34 (0%)
# events			
Blood lactate dehydrogenase increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	1/34 (2.94%)
# events			
Creatinine renal clearance decreased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	4/34 (11.76%)
# events			
Gamma-glutamyltransferase increased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	0/34 (0%)
# events			
Haemoglobin decreased † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	0/61 (0%)	2/34 (5.88%)
# events			
Transaminases increased † A			
# participants affected/at risk	1/8 (12.5%)	1/61 (1.64%)	0/34 (0%)
# events			
Weight decreased † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	9/61 (14.75%)	2/34 (5.88%)
# events			
Metabolism and nutrition disorders			
Decreased appetite † <sup>A</sup>			
# participants affected/at risk	3/8 (37.5%)	13/61 (21.31%)	7/34 (20.59%)
# events			
Hypokalaemia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	3/34 (8.82%)
# events			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
Hyponatraemia † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	1/61 (1.64%)	0/34 (0%)
# events			
Musculoskeletal and connective tissue disorders			
Arthralgia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	3/34 (8.82%)
# events			
Back pain † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	1/34 (2.94%)
# events			
Muscle spasms † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	2/34 (5.88%)
# events			
Musculoskeletal pain † <sup>A</sup>			
# participants affected/at risk	1/8 (12.5%)	5/61 (8.2%)	1/34 (2.94%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# events			
Myalgia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	2/34 (5.88%)
# events			
Neck pain † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	0/34 (0%)
# events			
Pain in extremity † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	3/34 (8.82%)
# events			
Nervous system disorders			
Dizziness † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	9/61 (14.75%)	4/34 (11.76%)
# events			
Dysgeusia † <sup>A</sup>			
# participants affected/at	0/8 (0%)	4/61 (6.56%)	2/34 (5.88%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
risk			
# events			
Headache † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	3/34 (8.82%)
# events			
Peripheral sensory neuropathy † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	2/34 (5.88%)
# events			
Psychiatric disorders			
Anxiety † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	3/34 (8.82%)
# events			
Sleep disorder † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	0/34 (0%)
# events			
Renal and urinary			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
disorders			
Urinary retention † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	1/61 (1.64%)	2/34 (5.88%)
# events			
Respiratory, thoracic and mediastinal disorders			
Cough † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	6/61 (9.84%)	6/34 (17.65%)
# events			
Dyspnoea † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	8/61 (13.11%)	8/34 (23.53%)
# events			
Epistaxis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	13/61 (21.31%)	8/34 (23.53%)
# events			
Haemoptysis † <sup>A</sup>			
# participants affected/at	0/8 (0%)	3/61 (4.92%)	2/34 (5.88%)

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
risk			
# events			
<b>Skin and subcutaneous tissue disorders</b>			
Alopecia † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	3/34 (8.82%)
# events			
Dry skin † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	1/34 (2.94%)
# events			
Erythema † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	2/61 (3.28%)	2/34 (5.88%)
# events			
Hair colour changes † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	0/34 (0%)
# events			
Night sweats † <sup>A</sup>			

	Pazopanib 600 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Pazopanib 800 mg Plus Pemetrexed 500 mg/m <sup>2</sup>	Cisplatin 75 mg/m <sup>2</sup> Plus Pemetrexed 500 mg/m <sup>2</sup>
# participants affected/at risk	0/8 (0%)	3/61 (4.92%)	2/34 (5.88%)
# events			
Palmar-plantar erythrodysesthesia syndrome † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	4/61 (6.56%)	1/34 (2.94%)
# events			
Pruritis † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	5/61 (8.2%)	1/34 (2.94%)
# events			
Rash † <sup>A</sup>			
# participants affected/at risk	0/8 (0%)	11/61 (18.03%)	5/34 (14.71%)
# events			
Vascular disorders			
Hypertension † <sup>A</sup>			
# participants affected/at risk	2/8 (25%)	18/61 (29.51%)	4/34 (11.76%)
# events			

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

## More Information

### Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

### Limitations and Caveats:

Efficacy data were only summarized for the pazopanib (pazo.) 800 mg + pemetrexed (peme.) 500 mg/m<sup>2</sup> and the cisplatin 75 mg/m<sup>2</sup> + peme. 500 mg/m<sup>2</sup> arms due to the small sample size/short treatment duration in the pazo. 600 mg + peme. 500 mg/m<sup>2</sup> arm.

### Results Point of Contact:

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